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How do I achieve diabetic remission in cats?
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The hallmark of diabetes is the presence of hyperglycemia. In contrast to acute hyperglycemia, chronic hyperglycemia impairs the secretion of insulin and contributes to insulin resistance and thereby perpetuates the diabetic disease. These damaging effects have been referred to as glucotoxicity, the cellular mechanisms of which are only partly understood. Amongst others inflammatory cytokines and oxidative stress seem to play an important role.

The concept of glucotoxicity is very important to understand because immediate treatment may reverse the negative effects of glucose and increase the chance of remission. Remission, which is defined as normalisation of blood glucose and fructosamine levels and resolution of clinical signs and glucosuria without further need of antidiabetic therapy, usually occurs within the first 3 months after initiating therapy. Up till now no tests have been established suitable to predict remission. Insulin concentrations (baseline levels as well as after IV glucagon or IV arginine) are usually low at the time of diagnosis because of the suppressive effects of glucose (1,2). Therefore, the appropriate approach is to aim for optimal metabolic control. Intermediate-acting insulins are insulins of first choice in cats with uncomplicated diabetes. A porcine derived lente-type insulin (Caninsulin) is licensed for use in cats in many countries and probably the insulin most often used. In some cats duration of insulin action is less than 12 hours, an additional issue is that insulin absorption may be inconsistent causing erratic blood glucose concentrations. In human diabetics the same problem exists, which has led to the recent development of insulin analogs. Insulin glargine (Lantus) is currently the most frequently used long-acting insulin analog. In cats the duration of action is longer for glargine than for lente-type insulins, however, duration is usually less than 24 hours and glycemic control is better when given twice daily instead of once daily (3). Insulin glargine may be a suitable alternative for cats in which duration of action of lente-type insulin is too short for metabolic control. It has been postulated that the remission rate is higher in cats treated with insulin glargine than with other types of insulin. Although our own results also showed an advantage of glargine (4) the number of published cases is still too small to allow a definitive conclusion.

Initial dosage (Caninsulin, Lantus) in cats weighing < 4 kg is 1 U/cat given twice daily, cats weighing > 4 kg usually receive 1.5 – 2.0 U/cat twice daily. In cats which have a blood glucose concentration < 20 mmol/l at the time of diagnosis, no more than 1 U/cat twice daily independent of the body weight is given.

The cat may be hospitalized for 1 – 2 days until work-up is completed. Blood glucose is measured 3 – 4 times throughout the day, insulin dosage should be reduced if hypoglycemia is detected (glucose < 5 mmol/l). Initial work-up and the begin of treatment may also be started on an outpatient basis.

The cat is a true carnivore which distinguishes it clearly from the omnivorous dog. The natural diet of wild felids such as mice and birds contains less than 10% of carbohydrates on a dry matter basis. Using low-carbohydrate-high-protein diet results in better clinical control and increased rates of diabetic remission (5). Time of feeding

relative to the insulin administration does not seem to play a role, the quality of metabolic control in cats receiving their meal together with the insulin injection is not different from cats which are fed 45 minutes after insulin administration (3). The feeding schedule should, however, be consistent from day to day, either two equal size meals around the time of insulin administration or “nibbling” throughout day and night.

Frequent re-evaluations and amendments of insulin dosage are essential to increase the chance of diabetic remission. In our hospital re-evaluations are performed 1,3,8,12 weeks after diagnosis and then approximately every 4 months. In most cats remission occurs during the first 3 months of therapy, if improvement of glycemic control or diabetic remission happen unnoticed serious hypoglycaemia may result. Ideally, fasting blood glucose (before the insulin injection) should be between 12-15 mmol/l and the nadir 5-9 mmol/l. Dosage changes are performed with increments of 0.5 U/cat BID approximately every 5 – 7 days. With this treatment regimen the current remission rate in our hospital is approximately 50%. Interestingly older cats have a greater chance of remission than younger cats (4).

We are currently exploring the effect of tight glycemic control during the first week after diagnosis of diabetes mellitus. The protocol includes continuous intravenous infusion of crystalline insulin and monitoring of interstitial glucose concentration with a continuous glucose monitoring system (Guardian REAL-time CGMS). We hypothesize that tight control of blood glucose levels is crucial for functional recovery of beta-cells in the early clinical stage of the disease. Preliminary results show that cats that started with the intensive insulin protocol are more likely to achieve remission than cats that started with the standard insulin therapy (71% vs. 50%, respectively).

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